

Claims Listing:

1. (original) A method for inducing melanogenesis in a human subject having an MC1R variant allele associated with loss of or diminished receptor function, which comprises the steps of administering to said subject an amount of an α -MSH analogue effective to induce melanogenesis by the melanocytes in the skin or other epidermal tissue of the subject.

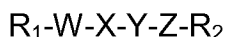
2. (original) The method of claim 1, wherein the α -MSH analogue is selected from:

(a) compounds of the formula:



wherein M is Met, Nle or Lys; and

(b) compounds of the formula:



wherein

R₁ is Ac-Gly-, Ac-Met-Glu, Ac-Nle-Glu-, or Ac-Tyr-Glu-;

W is -His- or -D-His-;

X is -Phe-, -D-Phe-, -Tyr-, -D-Tyr-, or -(pNO₂)D-Phe⁷-;

Y is -Arg- or -D-Arg-;

Z is -Trp- or -D-Trp-; and

R₂ is -NH₂; -Gly-NH₂; or -Gly-Lys-NH₂.

3. (original) The method of claim 1, wherein the α -MSH analogue is a cyclic analogue wherein an intramolecular interaction exists (1) between the amino acid residue at position 4 and an amino acid residue at position 10 or 11, and/or (2) between the amino acid residue at position 5 and the amino acid residue at position 10 or 11.

4. (original) The method of claim 3, wherein the intramolecular interaction is a disulfide bond or other covalent bond.

5. (original) The method of claim 1, wherein the α -MSH analogue is selected from the group consisting of:

Ac-Ser-Tyr-Ser-Nle-Glu-His-D-Phe-Arg-Trp-Lys-Gly-Pro-Val-NH₂

Ac-Ser-Tyr-Ser-Nle-Asp-His-D-Phe-Arg-Trp-Lys-Gly-Pro-Val-NH₂

Ac-Nle-Glu-His-D-Phe-Arg-Trp-Lys-Gly-Pro-Val-NH₂

Ac-Nle-Asp-His-D-Phe-Arg-Trp-Lys-Gly-Pro-Val-NH₂

Ac-Nle-Asp-His-D-Phe-Arg-Trp-Gly-NH₂

Ac-Nle-Glu-His-D-Phe-Arg-Trp-Lys-NH₂

Ac-Nle-Asp-His-D-Phe-Arg-Trp-Lys-NH₂

Ac-Nle-Glu-His-D-Phe-Arg-Trp-Orn-NH₂

Ac-Nle-Asp-His-D-Phe-Arg-Trp-Orn-NH₂

Ac-Nle-Glu-His-D-Phe-Arg-Trp-Dab-NH₂

Ac-Nle-Asp-His-D-Phe-Arg-Trp-Dab-NH₂


Ac-Nle-Glu-His-D-Phe-Arg-Trp-Dpr-NH₂


Ac-Nle-Glu-His-Phe-Arg-Trp-Lys-NH₂


Ac-Nle-Asp-His-Phe-Arg-Trp-Lys-NH₂


6. (original) The method of claim 1, wherein the α -MSH analogue is selected from the group consisting of:


Ac-Nle-Glu-His-D-Phe-Arg-Trp-Lys-Gly-Pro-Val-NH₂


Ac-Nle-Glu-His-D-Phe-Arg-Trp-Lys-NH₂


Ac-Nle-Asp-His-D-Phe-Arg-Trp-Lys-NH₂


Ac-Nle-Asp-His-D-Phe-Arg-Trp-Orn-NH₂



Ac-Nle-Asp-His-D-Phe-Arg-Trp-Dab-NH₂

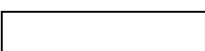



7. (original) The method of claim 1, wherein the α -MSH analogue is


[D-Phe⁷]- α -MSH,
 [Nle⁴, D-Phe⁷]- α -MSH,
 [D-Ser¹, D-Phe⁷]- α -MSH,
 [D-Tyr², D-Phe⁷]- α -MSH,
 [D-Ser³, D-Phe⁷]- α -MSH,
 [D-Met⁴, D-Phe⁷]- α -MSH,
 [D-Glu⁵, D-Phe⁷]- α -MSH,


[D-His⁶, D-Phe⁷]-α-MSH,
 [D-Phe⁷, D-Arg⁸]-α-MSH,
 [D-Phe⁷, D-Trp⁹]-α-MSH,
 [D-Phe⁷, D-Lys¹¹]-α-MSH,
 [D-Phe⁷, D-Pro¹²]-α-MSH,
 [D-Phe⁷, D-Val¹³]-α-MSH,
 [D-Ser¹, Nle⁴, D-Phe⁷]-α-MSH,
 [D-Tyr², Nle⁴, D-Phe⁷]-α-MSH,
 [D-Ser³, Nle⁴, D-Phe⁷]-α-MSH,
 [Nle⁴, D-Glu⁵, D-Phe⁷]-α-MSH,
 [Nle⁴, D-His⁶, D-Phe⁷]-α-MSH,
 [Nle⁴, D-Phe⁷, D-Arg⁸]-α-MSH,
 [Nle⁴, D-Phe⁷, D-Trp⁹]-α-MSH,
 [Nle⁴, D-Phe⁷, D-LYS¹¹]-α-MSH,
 [Nle⁴, D-Phe⁷, D-Pro¹²]-α-MSH,
 [Nle⁴, D-Phe⁷, D-Val¹³]-α-MSH,



 [Cys⁴, Cys¹⁰]-α-MSH



 [Cys⁴, D-Phe⁷, Cys¹⁰]-α-MSH


 [Cys⁴, Cys¹¹]-α-MSH


 [Cys⁵, Cys¹⁰]-α-MSH


 [Cys⁵, Cys¹¹]-α-MSH


 [Cys⁴, Cys¹⁰]-α-MSH₄₋₁₃


 [Cys⁴, Cys¹⁰]-α-MSH₄₋₁₂
 [Nle⁴, D-Phe⁷]-α-MSH₄₋₁₀,
 [Nle⁴, D-Phe⁷]-α-MSH₄₋₁₁,
 [D-Phe⁷]-α-MSH₅₋₁₁,
 [Nle⁴, D-Tyr⁷]-α-MSH₄₋₁₁,
 [(pNO₂)D-Phe⁷]-α-MSH₄₋₁₁,
 [Tyr⁴, D-Phe⁷]-α-MSH₄₋₁₀,
 [Tyr⁴, D-Phe⁷]-α-MSH₄₋₁₁,
 [Nle⁴]-α-MSH₄₋₁₁,
 [Nle⁴, (pNO₂)D-Phe⁷]-α-MSH₄₋₁₁,
 [Nle⁴, D-His⁶]-α-MSH₄₋₁₁,
 [Nle⁴, D-His⁶, D-Phe⁷]-α-MSH₄₋₁₁,
 [Nle⁴, D-Arg⁸]-α-MSH₄₋₁₁,
 [Nle⁴, D-Trp⁹]-α-MSH₄₋₁₁,
 [Nle⁴, D-Phe⁷, D-Trp⁹]-α-MSH₄₋₁₁,
 [Nle⁴, D-Phe⁷]-α-MSH₄₋₉, or
 [Nle⁴, D-Phe⁷, D-Trp⁹]-α-MSH₄₋₉.

8. (currently amended) The method of claim 1, wherein the α-MSH analogue is

[Nle⁴, D-Phe⁷]-α-MSH₄₋₁₀,
 [Nle⁴, D-Phe⁷]-α-MSH₄₋₁₁,
 [Nle⁴, ~~D-Phe⁷~~ D-Phe⁷, D-Trp⁹]-α-MSH₄₋₁₁, or
 [Nle⁴, D-Phe⁷]-α-MSH₄₋₉.

9. (original) The method of claim 1, wherein the α-MSH analogue is [Nle⁴, D-Phe⁷]-α-MSH.

10. (currently amended) A method of making a pharmaceutical preparation comprising
~~Use of an α-MSH analogue in the manufacture of a preparation for practicing the~~

method of claim 1 for inducing melanogenesis in a human subject having an MC1R variant allele associated with loss of or diminished receptor function.

11. (new) A method for inducing melanogenesis in a human subject having an MC1R variant allele associated with loss of or diminished receptor function, which comprises the steps of administering to said subject an amount of [Nle⁴, D-Phe⁷]- α -MSH effective to induce melanogenesis by the melanocytes in the skin or other epidermal tissue of the subject.

12. (new) A method according to claim 1 wherein the human subject has one or more variant alleles selected from the group consisting of Val60Leu (V60L), Asp84Glu (D84E), Val92Met (V92M), Arg142His (R142H), Arg 151Cys (R151C), Arg160Trp (R160W), and Asp194His (D294H).

13. (new) A method according to claim 1 wherein the human subject has two or more variant alleles selected from the group consisting of Val60Leu (V60L), Asp84Glu (D84E), Val92Met (V92M), Arg142His (R142H), Arg 151Cys (R151C), Arg160Trp (R160W), and Asp194His (D294H).

14. (new) A method according to claim 1 wherein the human subject has a Fitzpatrick skin type of I or II.

15. (new) A method according to claim 1 wherein the MC1R variant is identified using primer sequences selected from 5'-tggacaggactatggctgtg-3' (MC1R-1F – SEQ ID NO:1), 5'-tcttcagcacgctcttcat-3' (MC1R-1R – SEQ ID NO: 2), 5'-cttctacgcactgcgctacc-3' (MC1R-2F – SEQ ID NO: 3) and 5'-gctttaagtgtgctgggcag-3' (MC1R-2R – SEQ ID NO: 4).